REMARKS

Status of the Claims

Claims 91, 93, 94, 97 and 98 were pending in the subject application. By this Amendment, Applicants have amended claims 91, 93 and 94. Claim 93 was amended to be within a reasonable scope which correlates with the teachings of the specification and the known art. Support for amendments to claim 93 may be may be found inter alia in the specification, *e.g.*, at page 32, lines 26-32. Claim 94 was amended, as suggested by Examiner MacFarlane, to be more definite. Claim 91 was amended for proper antecedent basis commensurate with claim 93.

Applicants maintain that the amendments raise no issue of new matter and respectfully request that the amendment be entered. Accordingly, upon entry of this Amendment, claims 91, 93, 94, 97 and 98 will be pending and under examination.

Applicants respectfully request entry of these amendments in accordance with 37 C.F.R. 1.114, Request for Continued Examination (RCE) practice, which RCE is also filed herewith.

Examiner Interview

Applicants thank Examiner MacFarlane for allowing Applicants' representative, Mary Johnson, to discuss entry of these amendments and the Applicants' position with regard to the outstanding enablement rejection during a telephonic interview on April 25, 2011. Applicants' Statement of the Substance of the Interview was filed in the subject application on this same day, and the Examiner is respectfully requested to review and notify Applicants if any material inaccuracies are noted.

Claim rejection under 35 U.S.C. §112, first paragraph

In the Office Action, rejections of claims 91, 93, 94, 97 and 98 under 35 U.S.C. 112, first

paragraph are maintained for reasons related to scope of enablement. The Examiner concludes that one of ordinary skill in the art would not know how to use the invention commensurate in scope with the claims.

The Examiner alleges that the one of ordinary skill in the art would not know how to use the method of the invention to inhibit the binding of pro-NGF comprising "exposing said receptor" to said antibodies in an animal " in need of increased survival of neurons", and that there is insufficient guidance within both the active steps of the method or within the disclosure as to how a skilled artisan would identify such animals in need, and by what regimes said antibody is to be administered, with an expectation of success.

Applicants respectfully respect reconsideration of the claims in light of the amendments made herein. Without conceding the propriety of the rejection, but in an effort to advance prosecution, Claim 93 was amended to recite:

> "A method for inhibiting the binding of pro-NGF to a sortilin receptor, wherein said method comprises administering an inhibitorily effective amount of an antibody which binds to an extracellular part of said receptor to an animal suffering from neurons that are damaged by trauma or surgery, thereby inhibiting the binding of pro-NGF to said receptor."

The claims no longer read on "exposing said receptor" or "an animal in need of increased survival of neurons". The claimed invention reads on: inhibiting the binding of pro-NGF to a sortilin receptor, by delivering an inhibitory antibody (generated from an extracellular domain of the sortilin receptor), to an animal suffering from damaged neurons. Applicants specification makes it clear that the sortilin receptor contains extracellular domains that are important in the binding of molecules that inhibit its function, and by targeting the extracellular domains of such sortilin receptor, inhibition of pro-NGF can be achieved. The

entire amino acid sequence of the sortilin receptor, including identification of extracellular domains of sortilin, is taught in the specification, and given these starting materials it is expected that antibodies can be made without undue experimentation. Examples of such antibodies were previously discussed in the Office Action response filed March 23, 2010. The Examiner alleges, however, that the crux of the enablement rejection is not based on how to make inhibitory antibodies, but that one skilled in the art would not know how to use the method of the invention.

The claimed invention now reads on administering such inhibitory antibody to an animal suffering from neurons that are damaged by trauma or surgery. The specification teaches this use, *e.g.,* at page 32, lines 26-32, and the Applicants maintain that the skilled artisan is enabled to practice the invention, *i.e.* make sortilin antibodies and administer such antibodies. It is understood that pro-neurotrophins play a role in apoptosis of neurons, especially during a state of injury. See, *e.g.*, the specification at page 3, lines 15-22. Also, the art teaches that antibodies can enter the central nervous system (CNS (cross blood-brain barrier (BBB)), especially when the BBB is damaged by trauma (injury) or surgery, or otherwise in a compromised state.

Applicants' Declaration of Dr. Castrén (filed June 15, 2009) provides evidence of increased survival of neurons in an animal model of spinal cord injury (surgery), wherein an inhibitor of sortilin is administered; and also an antibody that is a strong inhibitor of sortilin receptor. The conditions used in the experiments of the Declaration are commensurate in scope with the specification as filed and what was well known to one of skill in the art. Such a showing is also commensurate with the scope of the claimed invention, *i.e.,* one which must bear a reasonable correlation to the scope of the claimed invention. (See the MPEP at 2164.08.)

The animal model of spinal cord injury used in the experiments of the Declaration was known at the time of filing the application. As noted in the scientific article of Harrington et

al., 2004, (referenced in the Declaration of Dr. Castrén; and submitted herewith in an Information Disclosure Statement (IDS)), "the procedure of stereotactic coordinates for internal-capsule lesion, fast blue labeling of CSN, and intracortical delivery of solutions in rats have been described (7)." (See the last three sentences of the first column on page 6230 of Harrington). Harrington, 2004, is referring to reference citation number 7 which is a paper by Geihl published in 1996, well before Applicants' filing date. As further evidence that animal models of CNS injury were well-known and studied, Beattie et al., 2002, (see also the instant specification at page 3, lines 20-22; and the IDS submitted herewith) describe a spinal cord injury experiment where pro-NGF antibodies were successfully administered.

If a statement of utility in the specification contains within it a connotation of how to use, and/or the art recognizes that standard modes of administration are known and contemplated, 35 U.S.C. 112 is satisfied. In re Johnson, 282 F.2d 370, 373, 127 USPQ 216, 219 (CCPA 1960); In re Hitchings, 342 F.2d 80, 87, 144 USPQ 637, 643 (CCPA 1965). See also In re Brana, 51 F.2d 1560, 1566, 34 USPQ2d 1437, 1441 (Fed. Cir. 1993).

For example, it is not necessary to specify the dosage or explicit instructions on how to administer, if it is known to one skilled in the art that such information could be obtained without undue experimentation.

Further, with regard to use of antibodies, Applicants previously filed a Declaration of Dr. Thomas Willnow on March 24, 2008 (the "Willnow Declaration") which describes the knowledge of the skilled artisan on successful use of antibodies, both pre-filing and subsequent to the filing of the application (see pages19-23 of the Willnow Declaration). References by Arshavsy (2006), Ballabh (2004), DeBoer (2006), Friden (1991), Neuwelt (2004) and Rubin (1999) were previously made of record in the application in a June 15, 2009 IDS. The Willnow Declaration describes how trauma, injury and/or disease

compromise the integrity of the blood-brain-barrier (BBB), and therefore a reasonable expectation of success using the antibodies of the invention exists.

In conclusion, as long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112 is satisfied. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

Applicants maintain that the claims embrace a reasonable scope commensurate with the specification and the state of the art at the time of filing. Accordingly, Applicants respectfully request that the enablement rejection be withdrawn.

For the forgoing reasons, Applicants believe that the application is now in condition for allowance. Such allowance is earnestly solicited.

If a further telephone interview would be of assistance in advancing prosecution of the present application, the Examiner is invited to telephone the undersigned at the number provided below. Appropriate fees for extension of time and for the concurrently filed RCE were submitted. No other fee is deemed necessary in connection with the filing of this Amendment and Response, however, authorization is hereby given to charge any underpayment, or credit any overpayment, to Deposit Account No. 50-3201.

Respectfully submitted,

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